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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,104	04/28/2005	Yong Kwee	053466-0401	5920

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EXAMINER	
SANG, HONG	
ART UNIT	PAPER NUMBER
1643	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,104	KWEE ET AL.	
	Examiner	Art Unit	
	Hong Sang	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *4-11 and 15-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 12-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 April 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/28/05 and 6/23/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RE: Kwee et al.

1. Applicant's election with traverse of Group I (claims 1-3 and 12-14) in the reply filed on 5/24/07 is acknowledged. The traversal is on the ground(s) that the claims of the remaining groups (Groups II-VI) are sufficiently related to be examined together, and that such examination would not place an undue burden on the Examiner. This is not found persuasive because the instant case is a national stage filing of an international application (i.e. 35 U.S.C. 371) and therefore the standard of burdensome search is not applied. As indicated in the last office action, the special technique feature liking the claimed inventions appeared to have been the HM1.24 protein. Because the technical feature linking the inventions is not novel and does not provide contribution over the prior art, the separation of claims into different groups was deemed proper and is therefore made FINAL.

2. Claims 1-22 are pending. Claims 4-11 and 15-22 are withdrawn from further consideration as being drawn to non-elected inventions.

3. The information disclosure statements (IDS) filed on 4/28/05 and 6/23/06 have been considered. Signed copies are attached hereto.

4. Claims 1-3 and 12-14 (wherein said HM1.24 is an HM1.24 protein or an HM1.24 peptide) are under examination.

Priority

5. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Objections

6. Claims 1, and 12-14 are objected to because of the following informalities: claims contain non-elected invention, i.e. HM1.24 DNA and HM1.24 RNA. Appropriate correction is required.

7. Claim 12 is objected to because of the following informalities: claim 12 contains a typographical error. The term "to-claim 1" should be "to claim 1". Appropriate correction is required.

Claim Rejections - 35 USC § 112, 1st paragraph

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-3 and 14-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antigen-specific dendritic cell pulsed by an HM1.24 protein or an HM1.24 peptide, does not reasonably provide enablement for a cancer vaccine containing as an active ingredient an antigen-specific dendritic cell pulsed by an HM1.24 protein or an HM1.24 peptide. The specification does not enable

any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)).

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in In re Wands, 8 USPQ2d 1400 (CA FC 1988). Wands states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

Claims are drawn to a cancer vaccine containing as an active ingredient an antigen-specific dendritic cell pulsed by an HM1.24 protein or an HM1.24 peptide.

The invention is in a class of invention, which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The breadth of the claims

Because the claims recite the term "vaccine", which means a preparation for preventing a disease, the invention is intended for preventing a cancer.

Quantity of experimentation

The quantity of experimentation in this area is extremely large given the fact that no material has been found to date that is capable of preventing a cancer.

The unpredictability of the art and the state of the prior art

Claims recite the word "vaccine". The broadest reasonable interpretation of the claims in this situation is to prevent a cancer.

No material has been found to date that has been shown to or would be expected to prevent cancer, and there is no working example, prior art, or any evidence that would provide the skilled artisan with any predictable guidance to use the claimed invention, it would be reasonable to conclude the claimed invention is not enabled.

Reasonable guidance with respect to preventing any cancer relies on quantitative analysis from defined populations that have been successfully pre-screened and are predisposed to particular types of cancer. This type of data might be derived from

widespread genetic analysis, cancer clusters, or family histories. The essential element towards the validation of a preventive therapeutic is the ability to test the drug on subjects monitored in advance of clinical cancer and link those results with subsequent histological confirmation of the presence or absence of disease. This irrefutable link between antecedent drug and subsequent knowledge of the prevention of the disease is the essence of a valid preventive agent. Further, a preventive administration also must assume that the therapeutic will be safe and tolerable for anyone susceptible to the disease.

Stevenson teaches that dendritic cells loaded with protein, peptides, or tumor-derived RNA have shown some clinical effects (Curr. Opin. Oncol., 2005, 17:573-577, see page 575, 2nd column). Komenaka et al. teach that in phase I trials using DCs in the treatment of patients with metastatic melanoma, autologous DCs were generated ex vivo and pulsed with class I restricted peptides, a number of patients demonstrated DTH responses to peptides or tumor lysates (Clinics in Dermatology, 2004, 22: 251-265, see page 259, right column). However, nowhere in the art does it show that tumor antigens are effective at preventing cancer.

Evans *et al* (Q. J. Med 1999: 92: 299-307) teach that vaccines against cancer are not fully established, and it is stated that adjuvant therapy to prevent or delay disease still needs experimentation. Evans *et al* further state that such cancer vaccines are at best used as a therapeutic and not as a prophylactic and that *"the notion that cancer vaccines will replace standard therapeutic strategies in malignant disease still belongs to the realm of fiction"* (see page 303 last paragraph).

Therefore the art has only recognized the treatment of a cancer.

Working examples

The specification shows the effectiveness of stimulation of T cells in vitro by dendritic cells pulsed with HM1.24 (see Example 1). The specification teaches that the HM1.24 specific T cells possess cytolytic activity in vitro (see Example 2). However, specification does not provide any data indicating that the dendritic cells pulsed with HM1.24 is capable of preventing any cancer.

Guidance in the specification

The specification provides insufficient guidance and objective evidence to indicate to one of skill in the art that the administration of the claimed dendritic cells pulsed with HM1.24 protein or peptide would be enabling to prevent cancer. Thus, given the fact that no material has been found to date that is capable of preventing a cancer, it would require undue experimentation to practice the instant invention as broadly claimed.

Level of skill in the art

The level of skill in the art is deemed to be high.

Conclusion

Thus given the broad claims in an art whose nature is identified as unpredictable,

the unpredictability of the art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the presence of a working example which does not address the issue of preventing cancer using claimed dendritic cells and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 1-3 and 12-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Treon et al. (Semin. Oncol. 2000, 27(5): 598-613, IDS) in view of Ohtomo et al. (Biochem. Biophy. Res. Commun., 1999, 258:583-591, IDS), and Porgador et al. (J. Exp. Med., 1995, 182: 255-260, IDS).

Treon et al. teach immunotherapeutic strategies for treatment of plasma cell malignancies such as multiple myeloma (MM) including immunization with functional dendritic cells pulsed with whole tumor antigen (see page 604, left column). Treon et al. teach that dendritic cells can be used to present myeloma associated peptides (see page 604, left column). Treon et al. teach that HM1.24 is expressed on MM patient

plasma cells and myeloma cell lines (see page 601, last paragraph). Treon et al. teach that HM1.24 is one of the typical candidate targets for antibody-mediated therapy of MM (see page 599, left column line 3).

Treon et al. do not specifically describe dendritic cells pulsed with HM1.24 protein or HM1.24 soluble peptide. However, these deficiencies are made up for in the teachings of Ohtomo and Porgador.

Ohtomo et al. teach that HM1.24 antigen has been identified as a surface molecule preferentially expressed on terminally differentiated B cells and its overexpression is observed in multiple myeloma cells (see abstract). Ohtomo et al. that the HM1.24 antigen is expected as a most potent target molecule for antibody-based immunotherapy for multiple myeloma (see abstract). Ohtomo et al. teach how to make soluble HM1.24 antigen (see page 584, last paragraph).

Porgador et al. teach a method of making dendritic cells pulsed with a class I-restricted peptide, wherein the peptides are small with 8 amino acid residues. These small peptides are soluble peptides.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make dendritic cells pulsed with HM1.24 protein or HM1.24 soluble peptide for treating multiple myeloma in view of the teachings of Treno, Ohtomo and Porgador et al. One would have been motivated to do so because Treon and Ohtomo et al. teach that HM1.24 antigen is overexpressed in multiple myeloma cells and is a most potent target for antibody-based immunotherapy for multiple myeloma, and dendritic cells pulsed with small soluble antigenic peptides have been

widely used to treat cancer. One of ordinary skill in the art would have a reasonable expectation of success to make dendritic cells pulsed with HM1.24 protein or HM1.24 soluble peptide for treating MM because the method of making dendritic cells pulsed with whole tumor antigen or small soluble antigenic peptides is known in the art as shown by Treon et al. and Porgador et al.

For this rejection, the intended use i.e. a cancer vaccine, wherein the cancer is a cancer of an organ or a tissue which expresses an HM1.24 protein or peptide is not given patentable weight.

Conclusion

12. No claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hong Sang whose telephone number is (571) 272 8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Hong Sang, Ph.D.
Art Unit 1643
June 5, 2007

Primary Examiner